# Estimating the profile of responders to treatment in the phase 3 EXPAND trial: do different patients show benefits on different outcomes?

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## OBJECTIVE

Adopt an innovative statistical approach combining the concept of defining responders to a therapy according to their baseline profile evaluating multiple endpoints.

## BACKGROUND

Different clinical and demographic patient profiles may respond differently to treatment depending on the underlying pathophysiology driving a particular clinical outcome and a therapy's MOA.

## DESIGN/METHODS

This post-hoc analysis of EXPAND compared siponimod (n=1099) vs placebo (n=546) in SPMS. We generated a response score derived from baseline characteristics describing participants with a more pronounced treatment effect on each of 4 clinical endpoints (EDSS, T25FW, 9HPT, SDMT) and evaluated optimal division into nonresponders/responders according to Zhao L et al. 2013. For good generalization performance training-validation was replicated on 500 bootstrap samples.

## RESULTS

In the whole cohort, the effect of siponimod on time to confirmed progression for each of the 4 outcomes was: EDSS: HR=0.79, p=0.0103; 9HPT: HR=0.86, p=0.23; T25FW: HR=0.95, p=0.53; SDMT: HR=0.75, p=0.001. Four different responder profiles (RSP) were obtained and validated, all showing a significant interaction with treatment, thus defining responders to each of the 4 outcomes. Scores for each outcome were split between RSP and non-RSP. RSP associated to EDSS (n=341) had a HR=0.48 (p=0.001), vs non-RSP with HR=0.89 (p=0.308). RSPs associated to 9HPT (n=403) had a HR=0.52 (p=0.007) and non-RSP HR=1.05 (p=0.751); T25FW RSP (n=905) had a HR=0.74 (p=0.008), vs HR=1.23 (p=0.077) in non-RSP; while SDMT RSP (n=899) had a HR=0.58 (p=0.001) vs HR=1.00 (p=0.988) in non-RSP. Overall, 1290/1645(78%) patients were pronounced siponimod-treatment responders in ≥ one of the 4 clinical outcomes.

## CONCLUSIONS

This study emphasizes the relevance of evaluating treatment response on different aspects of MS. This methodology allows to depict patient profiles from baseline characteristics that are associated with higher treatment effects on individual outcomes. 78% of SPMS patients had a large treatment benefit with siponimod on at least one of the 4 clinical outcomes.